REMARKS

Reconsideration is respectfully requested. Claims 1-23, and 28 have been cancelled. Claims 24-27, 29-36 and 38-42 are pending and stand rejected.

Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections made by the Patent Office. Applicants reserve the right to pursue prosecution of any presently claim embodiments in future continuation and/or divisional applications.

Rejections under 35 USC § 103(a)

The Examiner has rejected the claims under 35 U.S.C. § 103(a) over numerous references.

Specifically, the Examiner has rejected claims 24-27, 29-31, 33, 34, 41, and 42 over U.S. Patent No. 5,320,808 to Holen *et al.* ("Holen") in view of U.S. Patent No. 5,532,128 to Eggers ("Eggers"). In addition, the Examiner rejects claim 32 over Holen and Eggers in further view of U.S. Patent No. 4,599,303 to Yabusaki ("Yabusaki"); claims 35, 36, 38, and 39 over Holen and Eggers in further view of U.S. Patent No. 5,780,234 to Meade ("Meade"); and claim 40 over Holen, Eggers, and Meade in further view of U.S. Patent No. 6,288,221 to Grinstaff ("Grinstaff").

Fundamentally, the obviousness rejections all rely on the combination of Holen and Eggers. The Examiner has failed to provide the requisite *prima facie* case for obviousness.

1. There is no motivation or suggestion to combine the references because the scientific principles of operation of the methods described by the references are incompatible.

The Examiner bears the burden of establishing that the cited references provide the requisite motivation or suggestion to combine their teachings. There must be some valid scientific principle or legal precedent supporting the combination of the methods taught by the reference. See M.P.E.P. § 2144. In the present case, the scientific principles of operation of

each of the references are incompatible with each other because combination of the teachings of Holen and Eggers would not result in a functional device.

Holen teaches methods of optically detecting a target analyte. In its summary of the invention, Holen discloses that the "reaction well is configured to provide direct optical access to the test sites." (Holen, Col. 4, lines 59-60). The test wells rotate to provide "desirable agitation of the fluids in a reaction wells" to allow different biochips to be analyzed (Holen, Col. 6 lines 45-50). The rotational system of Holen detects compounds in the system by using an optical reader that:

> emits a beam of optical radiation onto a small portion of the test site ... [T]he optical detector converts the intensity of the optical radiation reflected by the diffuse surface of the test site into the electrical signal. The signal is then processed to obtain the optical density value of the test site 84 which is directly related to the concentration of the binding component of interest in the biological sample.
> Holen, Column 8, lines 21-29.

In Holen, the signal is thus detected remotely from the detection wells. Processing the optical signal in the Holen system is accomplished without attaching electrically conductive contacts attached directly to the detection wells.

Eggers, by contrast, teaches detecting the presence of analytes by measuring changes in chemoelectrical properties in a sample. Eggers discloses measuring changes in electrical properties that require electrical contacts such as frequency ranges, conductance, and permittivity. (e.g. Eggers, Col. 5, lines 54-62). Specifically, Eggers teaches that "[c]hanges in the dielectric properties formed by the test sites 14 of FIGS. 2a-b are detected by detection circuitry 16." (Eggers, col. 4, lines 61-63). Detecting changes in electrical properties in separate wells requires attachment of electrical contacts directly to each separate well. Eggers does not teach inserting first and second biochips into a device as claimed.

The electrochemical properties detected according to Eggers cannot be detected in the rotationally based optical system taught by Holen. In Eggers, electrochemical detection of the samples require that electrical contacts must be maintained with each sample of each biochip. Maintaining separate electrical contacts measuring separate signals in each well in the Eggers system would not be possible in a rotational system of Holen because the samples freely rotate away from the Holen detector. The system would thus not maintain electrical contact with each of the wells. The electrochemical properties detected in Eggers thus could not be detected in the rotational system of Holen.

The electrochemical methods of Eggers are also not adaptable to the rotational system of Holen because the samples would be agitated in a manner incompatible with electrochemical measurements. The samples in the Eggers reference must conduct electric signals to a detector to detect changes in electrochemical properties. Holen expressly teaches that the carousel is arranged "to provide agitation required for processing samples and reagents." (Holen, Col. 6, lines 29-31). Further, Holen describes the carousel containing the samples "disposed on a tilted axis." (Holen, Col. 6, lines 45-46). Fluid agitation on a tilted axis requires the presence of air in a sample. Like all non-conducting materials, air does not allow electrical conductivity such as that necessary in the electrochemical detection method of Eggers. As such, Holen could not be adapted to use the electrochemical detection methods of Eggers.

In addition, none of the additional references (Yabusaka, Meade, and Grinstaff) provide a scientific basis to combine electrochemical methods in first and second biochips, as claimed. None of the references teach multiple biochips, and none of the references provide guidance in how to overcome the technical limitations of Holen that render electrochemical detection impossible.

Because the scientific principles of operation of each of the cited references are incompatible, there is no motivation or suggestion to combine the references.

Examiner's Arguments

The Examiner argues that one or ordinary skill in the art would have been motivated to combine the references, stating that:

> Eggers teaches the advantages of the disclosed electronic detection apparatus and methodology in relation to optical detection methods utilizing fluorescent labels and including intercalating dyes for DNA analysis (see col. 2, lines 1 – col. 3, lines 26).

However, as pointed out above, the electrochemical design disclosed by Eggers could not be adapted to the device of Holen. While Eggers show the advantages of electrochemical detection in a single detection well, Eggers fails to show how this perceived advantage could be accomplished using the rotational system of Holen that not only does not require maintenance of electrical contact between the samples and the detection system, but also tilts and agitates samples in a manner wholly incompatible with the methods taught by Eggers.

The Examiner also states that

> [t]he strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination.

As discussed above, there is no scientific basis for combining the references because the methods of Holen and Eggers are incompatible. Further, there is also no legal precedent supporting the combination of the particular references.

The Examiner has failed to provide the requisite motivation to combine the incompatible references to make the claimed invention.

2. The combined references do not provide a reasonable expectation of success of combining the optical detection device of Eggers with the electrical detection based device of Holen.

As discussed above, the methods taught by Holen are incompatible with those taught by Eggers.

First, one of ordinary skill in the art would not have a reasonable expectation of combining the electrochemical detection methods taught by Eggers with the rotating system of Holen because electrical contacts cannot be maintained to each of the samples. In Holen, the signal is detected remotely from the detection wells in a rotating system. Maintaining separate electrical contacts measuring separate signals in each well in the Eggers system would not be possible in a rotational system of Holen because the electrical leads would not remain in contact with the samples. As such, one of ordinary skill in the art would not have a reasonable expectation of success in combining the methods taught by Eggers with those of Holen.

Further, one of ordinary skill in the art would not have a reasonable expectation of combining the references to make the claimed invention because agitating of the samples as taught by Holen does not allow electrochemical detection as taught by Eggers. As discussed above, Eggers must maintain conductive contacts between the sample and the detector in order to measure changes in electrochemical properties of the sample. Holen expressly teaches that the carousel is arranged "to provide agitation required for processing samples and reagents." (Holen, Col. 6, lines 29-31). Further, Holen describes the carousel containing the samples "disposed on a tilted axis." (Holen, Col. 6, lines 45-46). Fluid agitation in samples placed on a tilted axis requires the presence of air in a sample. Like all non-conducting materials, air does not allow electrical conductivity in samples such as that necessary in the electrochemical detection method of Eggers. Accordingly, one of ordinary skill in the art would not have a

reasonable expectation of success in conducting electrochemical detection as described by Eggers in the methods taught by Holen.

Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness and request that the various rejections under 35 U.S.C. §103(a) be withdrawn.

Conclusion

The present application is therefore in condition for allowance. Early and favorable notification thereof is respectfully requested. If the Examiner believes there are further unresolved issues, the Examiner is invited to call the undersigned at (415) 781-1989.

Respectfully submitted,

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